

Parameters associated with survival in patients undergoing surgical treatment due to rectal cancer

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Abstract

Aim: Colorectal cancer is the third most common type of cancer. Approximately 1/3 of colorectal cancers are rectum cancers. The percentage of local disease stage is 39%, and the 10-year survival rate in such patients is approximately 90%. The aim of our study was to evaluate the relationship between the clinicopathological characteristics and survival of patients with rectal cancer.

Material and Methods: Patients who had undergone surgical treatment for rectal cancer in our clinic between January 2008 and December 2013 were evaluated retrospectively. The effects of clinicopathological parameters of these patients on survival were investigated. The preoperative and postoperative variables were evaluated together with survival data.

Results: Of the 70 patients, 30 (43%) were females and 40 (57%) were males. The median age was 61 years (min-max = 29-87 years). Eight of the patients (6%) were operated under emergency conditions due to acute abdomen or ileus. 13 (19%) of the patients had undergone laparoscopic surgery and 57 (81%) had undergone open surgical resection. 15 patients (21%) had undergone anterior resection (AR), 51 (73%) had lower anterior resection (LAR) and 4 (6%) had abdomino-perineal resection (APR). According to pTNM staging, 6 patients (8%) were at stage-0, 7 (10%) were at stage-I, 22 (32%) were at stage-II, 26 (37%) were at stage-III, and 9 (13%) were at stage IV.

Conclusion: We found that the ASA (American society of Anesthesiologists) score height, final stage of the tumor and vascular (venous) invasion associated with overall survival

Keywords: Rectal Cancer; Survival; Surgery.

INTRODUCTION

Colorectal cancer is the third most common type of cancer. More than 1 million people are diagnosed with colorectal cancer every year in the world. Approximately 1/3 of colorectal cancers are rectum cancers (1). While the 5-year relative survival rate in colorectal cancer is 65%, the 10-year survival rate decreases to 58%. The percentage of local disease stage is 39%, and the 10-year survival rate in such patients is approximately 90% (2). The aim of our study was to evaluate the relationship between the clinicopathological characteristics and survival of patients with rectal cancer.

MATERIAL and METHODS

Patients who had undergone surgical treatment for rectal cancer in our clinic between January 2008 and

December 2013 were evaluated retrospectively. The effect of clinicopathological parameters of these patients on survival was investigated. The preoperative and postoperative variables were evaluated together with survival data. This study was carried out after approval from the Firat University School of Medicine Non-Interventional Ethics Committee with the decision number & date of 16543 & December 13, 2014.

In this study, patients with stage I, II, III or IV rectal cancer having upper, middle and lower rectum tumors, who had undergone curative rectal surgery, were included in the study. Patients who had undergone surgery for palliation were excluded from the study.

The demographic parameters, preoperative clinical and laboratory data, operative findings, histopathological

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findings of the surgical specimen and the postoperative follow-up data of the patients were evaluated (Table 1).

All patients' data were retrospectively obtained from the digital medical patient files and the outpatient clinic files of the follow-up period.

The relationship of survival with the patient's age, sex, ASA (American Society of Anesthesiologists) score, tumor location, preoperative stage, tumor size, serum CEA (carcinoembryonic antigen) levels, surgical technique,

neo-adjuvant treatment administration, perioperative M stage, surgical margin status and surgical margin distance, tumor diameter, the number of lymph nodes removed, T and N stages, differentiation, tumor invasion status, pathological stage and adjuvant treatment were evaluated. The patient's sex, tumor size, T and N stage, surgical margin status and differentiation parameters were analyzed in a multivariate analysis model (Table 2, 3 and 4).

Table 1. Demographics, clinical and pathological features of patients including; age, gender, ASA score, tumor site, preoperative CEA and hemoglobin levels, surgical types and technics, length of operation, stoma opening and type of stoma, differentiation and staging of the cancer

Age	61 (29-87)	Length of the specimen (cm±SD)	20±1
Gender		Size of the tumor (cm±SD)	4.2±0.3
Female	30 (43%)	Proximal margin (cm±SD)	12.7±0.9
Male	40 (57%)	Distal margin (cm±SD)	2.8±0.2
ASA Score*		Radial margin (cm±SD)	0.6±0.1
I	1 (0.7%)	Differentiation	
II	24 (34%)	well	6 (9%)
III	38 (38%)	moderate	46 (65%)
IV	7 (10%)	poorly	18 (26%)
Tumor location (rectum)		T stage**	
Distal	12 (17%)	T1	2 (3%)
Middle	23 (33%)	T2	12 (19%)
Proximal	35 (50%)	T3	26 (41%)
Preoperative CEA levels (IU/ml)		T4	24 (37%)
median	3 (0-215)	N Stage**	
mean±SD	11.0±3.9	N0	33 (52%)
Preoperative hemoglobin levels (g/dl)		N1	21 (33%)
mean±SD	12.6±0.2	N2	10 (15%)
Surgical technique		Pathological staging**	
Laparoscopy	13 (19%)	Stage 0	6 (8%)
Open	57 (81%)	Stage I	7 (10%)
Type of operation		Stage II	22 (32%)
Anterior resection	15 (21%)	Stage III	6 (37%)
Low anterior resection	51 (73%)	Stage IV	9 (13%)
Abdominoperineal resection	4 (6%)	Diverting stoma	47 (67%)
Length of operation (minutes) (min-max)	210 (90-380)	Ileostomy	44 (94%)
		Colostomy	3 (6%)

*According to American Society of Anesthesiologists, ASA score

**According to TNM classification of the American Joint Committee on Cancer (AJCC)

Table 2. Univariate analysis of parameters that can be effective on general survival by using Kaplan-Meier method

	p value		p value
Age (≤ 60 vs > 60)	0.9	Radial margin (≤ 2 vs > 2)	0.6
Gender (female vs male)	0.7	Radial margin positivity (+ vs -)	0.7
ASA (I, II, III, IV)*	0.005	Size of the tumor (cm) (≤ 4 vs > 4)	0.5
Tumor site (distal, middle, proximal)	0.8	Number of lymph nodes (≤ 12 vs > 12)	0.4
Preoperative distant metastasis (M+ vs M-)	0.001	Metastatic / total lymph nodes ratio	0.0001
Preoperative staging (I, II, III, IV)	0.009	Diameter of the greatest metastatic lymph node (mm) (≤ 5 vs > 5)	0.6
CEA (ng/ml) (≤ 5 vs > 5)	0.0001	T stage (T1, T2, T3, T4)**	0.2
CA 19-9 (U/ml)	0.0001	N stage (N0, N1, N2)**	0.2
Hemoglobin levels (g/dl)	0.001	Differentiation (well, moderately, poorly)	0.4
Type of operation (Emergency vs elective surgery)	0.02	Angiolymphatic invasion (present vs not present)	0.5
Neoadjuvant treatment (given vs not given)	0.4	Venous invasion (present vs not present)	0.1
Intraoperative distant metastasis (M+ & M-)	0.07	Crohn like lymphoid reaction (present vs not present)	0.3
Surgical technic (laparoscopic vs open)	0.5	Perineural invasion (present vs not present)	0.3
Type of operation (anterior resection, low anterior resection, abdominoperineal resection)	0.5	Pathological stage (0, I, II, III, IV)**	0.001
Length of the specimen (cm)	0.06	Adjuvant chemotherapy (given vs not given)	0.6
Proximal margin (cm) (≤ 10 vs > 10)	0.3	Adjuvant radiotherapy (given vs not given)	0.3
Distal margin (cm) (≤ 2 vs > 2)	0.6	Type of adjuvant chemotherapy (5-Fluorouracil / leucovorin, Others)	0.8
Distal margin (cm) (≤ 1 vs > 1)	0.6		

*According to American Society of Anesthesiologists, ASA score

**According to TNM classification of the American Joint Committee on Cancer (AJCC)

Table 3. Multivariate analysis of parameters that can effect on general survival by using the Kaplan-Meier method

Parameters	p value
Gender	
Female vs male	0.3
Size of tumor (cm)	
< 4 cm vs ≥ 4 cm	0.2
T stage*	0.01
N stage*	0.04
Differentiation	0.4
Surgical margins	0.5

*According to TNM classification of the American Joint Committee on Cancer (AJCC)

Table 4. Multivariate analysis of parameters that can be effective on general survival by using Cox Proportional Hazards model

Parameters	p value	Hazard ratio	CI
Stage			
stage IV vs I	0.002	9247	26-637000
ASA score			
ASA 4 vs 2	0.002	4135	21-1660000
Type of operations			
Emergency vs elective surgery	0.2	4	2-16
Preoperative CEA levels			
CEA > 5 vs < 5	0.5	2	0.5-28
Venous invasion			
Yes vs no	0.0001	107	9-3300

Statistical Analysis

All data were analyzed using the SPSS Statistics for Windows, Version 22 (IBM Corp, Armonk, New York) and p values of < 0.05 were considered to be statistically significant. The chi-square test was used for the analysis of the qualitative data. The Mann-Whitney U test was used for the analysis of the quantitative data. In addition to the descriptive statistical methods (mean, standard deviation, and frequency), the univariate and multivariate analysis, the Kaplan-Meier cumulative survival analysis and the 'average survival' analysis by Cox Proportional Hazards Model were carried out to analyze the data.

RESULTS

Of the 70 patients with rectal cancer who had been operated for curative purposes, 30 (43%) were females and 40 (57%) were males. The median age was 61 years (min-max = 29-87 years). One patient (1%) was in ASA-I, 24 (34%) were in ASA-II, 38 (54%) were in ASA-III and 7 (10%) were in the ASA-IV risk category. Twelve (17%) of the tumors were located in the distal region (0-5 cm), 23 (33%) in the mid-region (6-10 cm), and 35 (50%) in the proximal region (> 10 cm) of the rectum. The median serum CEA in the preoperative period was 3 IU/ml (min-max = 0-215 IU/ml), and the mean was 11.0 ± 3.93 IU/ml. The mean preoperative Hemoglobin level was 12.6 ± 0.2 g/dl. Neoadjuvant chemoradiotherapy (CRT) had been administered in 24 (34%) patients. All patients who received neoadjuvant CRT treatment received long-term ($1.8 \times 28 = 50.4$ Gy + 5-FU, for 28 days) fractional

CRT treatment. Chemoradiotherapy was administered to patients with T3, T4 and/or N + in clinical TNM staging. All patients had undergone the surgical operation between the 6th and 8th week after the cessation of neoadjuvant CRT treatment. Of the 24 patients who had undergone neoadjuvant CRT, 15 (68%) had radiological (computed tomography, magnetic resonance) primary tumor response. Eight of the patients (6%) were operated under emergency conditions due to acute abdomen or ileus. 13 (19%) of the patients had undergone laparoscopic surgery and 57 (81%) had undergone open surgical resection. 15 patients (21%) had undergone anterior resection (AR), 51 (73%) had lower anterior resection (LAR) and 4 (6%) had abdomino-perineal resection (APR). Seven (10%) of the anastomoses were performed manually and 59 (90%) had been carried out with a stapler. The mean operation time was 210 ± 7 minutes (min-max = 90-380 minutes). Forty-one patients (67%) had a stoma, 44 (94%) of which were ileostomy and 3 (6%) were colostomy. Intra-abdominal metastasis had been detected in 5 (7%) of 70 patients preoperatively. Four (6%) of the operated patients died in the early perioperative period. The median hospital stay was 16 days (min-max = 5-62 days). The mean length of specimen was 20 ± 1 cm. The diameter of the primary tumor ranged from 0.5 to 11 cm. The mean tumor diameter was 4.2 ± 0.3 cm. The mean distance to the proximal surgical margin was 12.7 ± 0.9 cm, the mean distance to the distal surgical margin was 2.8 ± 0.2 cm, and the mean distance to the radial surgical margin was 0.6 ± 0.1 cm. On the pathological examination, the distal surgical margin was interpreted as positive in one patient ($n = 1/70$, 1.4%). The mean number of lymph nodes removed was 17 ± 1 (min-max = 1-52) in the whole study population and 26 ± 2 (min-max = 13-52) in patients who had not received neoadjuvant therapy. The mean number of metastatic lymph nodes was 2.1 ± 0.6 , and the ratio of the metastatic lymph node count to the total number of lymph nodes was 0.14 ± 0.03 . The diameter of the smallest lymph node removed was 0.2 cm, and the largest was 2.7 cm. When tumor differentiation was evaluated, 6 of the tumors (9%) were well-differentiated, 46 (65%) were moderately differentiated, and 18 (26%) were poorly differentiated. The distribution of the pathological T stage was as follows: 2 (3%) of the tumors were T1, 12 (19%) were T2, 26 (41%) were T3, and 24 (37%) were in stage T4. The distribution of the pathological N stage was as follows: 33 (52%) were N0, 21 (33%) were N1 and 10 (15%) were in N2 stage. 45 patients (78%) had an angiolymphatic invasion, 12 (21%) had venous invasion and 18 (32%) had a perineural invasion. The Crohn-like lymphatic reaction was present in 13 patients (25%) and mesenteric tumor nodules were detected in 15 patients (31%). According to pTNM staging, 6 patients (8%) were at stage-0, 7 (10%) were at stage-I, 22 (32%) were at stage-II, 26 (37%) were at stage-III, and 9 (13%) were at stage IV. Adjuvant chemotherapy was given to 28 patients and adjuvant chemoradiotherapy was given to 9 patients. The median follow-up period was 12 months (min-max = 1-58 months) and the median overall survival was 27 months.

There was no significant difference in survival between the age groups when the patients were divided into two groups as those younger and older than 60 years of age ($p = 0.9$). Forty (57%) of the patients were male. There was no statistically significant difference in survival between the genders ($p = 0.7$). We observed that the patients' ASA score had a statistically significant effect on the overall survival ($p = 0.005$). As the ASA score increased, survival was shortened. There was no significant relationship between tumor location and survival ($p = 0.8$). However, as expected, the presence of metastasis on computed tomography had a significant effect on survival ($p < 0.001$).

When the patients were divided into two groups according to the preoperative serum CEA level as those ≤ 5 IU/ml and > 5 IU/ml, there was a significant difference between the groups in terms of the overall survival ($p = 0.0001$). The preoperative serum CA 19-9 (Cancer antigen 19-9) levels were also significantly associated with survival. As the serum CA 19-9 level increased, survival was shortened ($p = 0.0001$). The preoperative low Hemoglobin values were also significantly associated with survival ($p = 0.001$).

There was no significant relationship between the surgical technique (AR-LAR-APR) and survival ($p = 0.5$) according to the univariate Kaplan-Meier survival analysis. We found that the open or the laparoscopic surgery technique was not associated with survival ($p = 0.5$). However, we found that elective surgery was significantly superior to the emergency surgical operation regarding survival ($p = 0.02$).

The survival was not significantly related to the distance of the tumor to the nearest proximal surgical margin (longer or shorter than 10 cm) ($p = 0.3$), to the distance to the closest distal surgical margin (longer or shorter than 2 cm) ($p = 0.6$), or to the closest distance to the radial surgical margin (longer than or shorter than 2 mm) ($p = 0.6$).

In the univariate Kaplan-Meier survival analysis, there was no significant relationship between the total number of lymph nodes removed (below 12 or above) and survival ($p = 0.4$). However, there was a significant relationship between the ratio of metastatic lymph nodes count / total lymph nodes removed and survival ($p = 0.0001$).

There was no significant correlation between the tumor diameter and survival ($p = 0.5$) and the largest lymph node diameter (longer or shorter than 5 cm) and survival ($p = 0.6$). There was no significant relationship between survival and T-stage or N-stage ($p = 0.2$, for both). There was no significant relationship between tumor differentiation and survival ($p = 0.4$). The disease stage was found to significantly related to survival ($p = 0.009$). Survival was shortened as the preoperative disease stage increased.

According to histopathological examination, angiolymphatic invasion ($p = 0.5$), venous invasion ($p = 0.1$), Crohn-like lymphatic reaction ($p = 0.3$), perineural invasion ($p = 0.3$), and presence of tumor nodules ($p = 0.5$) were not significantly related to survival.

There was no significant relationship between adjuvant chemotherapy and survival ($p = 0.6$) and adjuvant CRT and survival ($p = 0.3$).

In the analysis with the multivariate Kaplan-Meier

model including gender, tumor size (<4 cm vs. ≥ 4 cm), T and N stage, surgical margin status and differentiation degree, T-stage ($p = 0.01$) and N-stage ($p = 0.04$) were independently associated with overall survival (Figure 1).

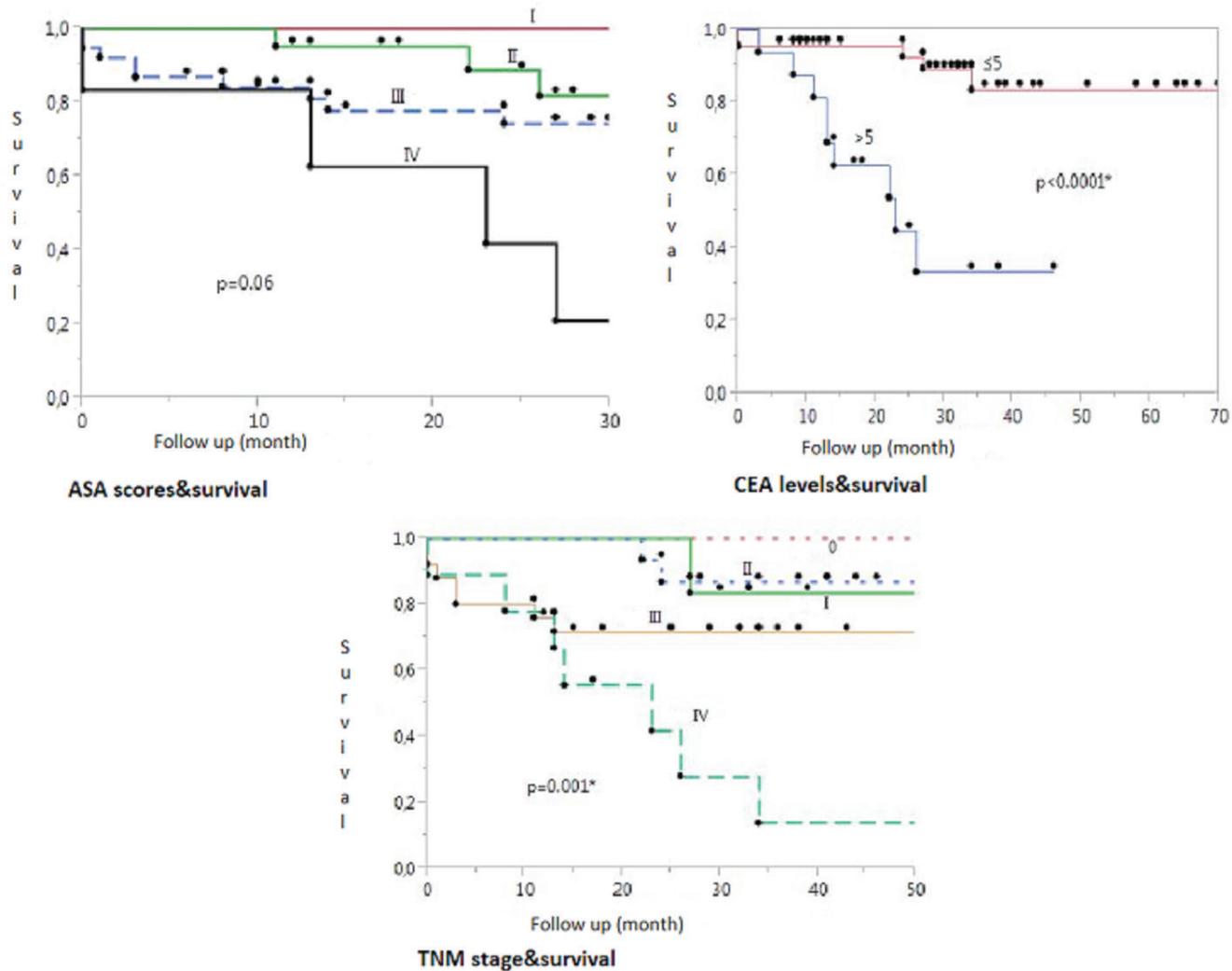


Figure 1. The relationship between 'ASA score, preoperative CEA value and TNM stage' and survival in Kaplan-Meier survival analysis

DISCUSSION

Rectum cancer is more common in men than in women with a rate of 3/2 (3). In our study, the male/female ratio was 4/3 in accordance with the literature.

Age is one of the major risk factors in sporadic colorectal cancers. The incidence increases from the fourth decade (3). In a study by Nasiri et al. (4) the authors divided the patients into two age categories, younger and older than 65 years of age, and found that age was a significant prognostic factor in terms of overall survival. On the other hand, Moghimi-Dehkordi et al. (5) reported that age was not a significant prognostic factor in their study population with colorectal cancer. In this study, the cut-off point was accepted as the age of 50 years. In our study, when we performed univariate and multivariate analyses of 2 groups based on the age of 60 years, we found that

the patient age was not significantly associated with overall survival.

In a study of 887 patients undergoing colorectal cancer surgery by Ragg et al. (6), being in the ASA III-IV group was reported to be an independent risk factor for mortality and morbidity. Gallina et al (7) found that the ASA score correlated with morbidity but it was not significantly related to mortality in their study including 328 patients. In our study, we determined that the ASA score of the patients was significantly correlated with overall survival and that survival was shortened as the ASA score increased. Localization of the tumor is an important factor in the choice of surgical treatment. The extent of resection and the level of the anastomosis are decided according to the localization of the rectum tumor. Mehrkhani et al. (4) reported that the site of the tumor was not associated with survival. In our study, 50% of the patients had a tumor

located in the proximal rectum and tumor localization had no statistically significant effect on survival.

Tumor markers are biological agents that are thought to be released from tumor cells and have a place in the patient follow-up in terms of diagnosis, evaluation of response to treatment, and detection of relapse (8). The most commonly used serum biomarkers for rectal cancer are carcinoembryonic antigen (CEA) and cancer antigen 19-9 (CA 19-9). CEA is the most widely used tumor marker as a pre-operative tumor marker. The prognosis of patients with a serum CEA level of > 5 ng/mL is poorer than those with < 5 ng/mL regardless of the disease stage (9). In a study of 572 patients with colorectal cancer (10), univariate and multivariate analyzes of pre-operative serum CEA and CA 19-9 levels showed that the serum CEA level was an independent prognostic factor, while CA 19-9 level was not significantly associated with the overall survival. Park et al. (11) reported that pre-operative high serum CEA level significantly correlated with the overall survival. In our study, we observed that the high serum CA19-9 level was statistically significantly associated with overall survival. In addition, patients enrolled in our study were divided into two groups as CEA> 5 ng / mL and CEA ≤ 5 ng / mL; the overall survival time of patients with a serum CEA level of > 5 ng / mL was shorter, which is in accordance with previous studies in the literature.

An abdominopelvic computed tomography (CT) can demonstrate the regional tumor extension, lymph node and distant metastases, complications due to the tumor (e.g., perforation, fistula), and it is recommended to almost all patients with rectal cancer (12). In our study, abdominopelvic CT was performed preoperatively in all patients who had undergone surgery due to rectal cancer. In our study, we detected distant organ metastasis at the time of diagnosis in 10% of the patients included in the study, and we observed that the survival time of these patients was statistically significantly shorter than the others. Magnetic Resonance Imaging (MRI) and endorectal ultrasound (ERUS) are essential tools in preoperative clinical staging and provide valuable information for T and N staging of the disease in rectal cancer patients. However, ERUS is an operator-dependent modality (13,14,15). In our study, only four patients had undergone preoperative MRI due to the low quality of our MRI device and none of our patients had undergone ERUS due to unavailability of the device.

Today, neoadjuvant CRT is applied as standard treatment in locally advanced rectal cancer patients in most Eastern European countries, USA, and Turkey. It is used in rectal tumors showing extramural extension and/or in patients with regional lymph node involvement (16). In contrast, in northern European countries, extraperitoneal rectal cancers are usually treated preoperatively with RT followed by a surgical operation (17). In our study, all of 24 patients had received long-term neoadjuvant CRT, and 15 (68%) of these patients had radiological tumor response.

The tumor stage has been reported to be one of the

important prognostic factors in most studies. The 5-year survival after curative surgery has been reported as 80-90%, 50-60% and 30-40% for stage I, II and III disease, respectively (18). Mehrkhani et al. (4) showed the pathological stage as an independent prognostic factor. In addition, Dulk et al. (19) reported in a study published in 2007 that the TNM stage was an independent risk factor for overall survival. In the univariate analysis performed in our study, we found that the TNM stage of the tumor was significantly associated with survival. In addition, we found that T and N stages were statistically significantly associated with survival in the multivariate analysis, which was consistent with the literature. Approximately 20% of patients diagnosed with rectal cancer are found to have distant metastasis at the time of diagnosis and the 5-year survival is approximately 40% in patients with resectable stage-IV disease (2). In our study, the rate of patients with stage-4 cancer was 10%.

In terms of laparoscopic and open rectal surgery, the COREAN (20) and COLOR II (21) studies found that the outcome of both open surgical and laparoscopic methods was equal regarding the oncological results. However, the AlaCaRT (22) and ACOSOG Z6051 (23) studies could not demonstrate the non-inferiority of laparoscopic rectum surgery compared to open rectal surgery in terms of oncopathological outcomes. In the study of Leung et al., the outcome of patients with rectal cancer was compared between open and laparoscopic surgery and it was shown that there was no significant difference between the two techniques in terms of survival (24). Similarly, a meta-analysis published by Gao et al. including 11 studies and a total of 285 patients demonstrated that laparoscopic rectum surgery had similar results to open rectum surgery in terms of mortality (25). In our study, we did not find a statistically significant difference between the two surgical techniques.

Survival was reported to be higher in patients undergoing elective surgery compared to those undergoing emergency surgery (26). Consistent with the literature, the overall survival time of 8 patients who had undergone emergency surgery in our study was statistically significantly shorter than that of patients undergoing elective surgery.

There are many studies on the effect of tumor diameter on prognosis in the literature. Although some studies have shown that the tumor diameter affects survival, Park et al. (11) did not find a significant relationship between the tumor size and prognosis in their study with a total of 2230 patients. In our study, there was no effect of tumor size on the overall survival.

The primary aim of rectal surgery is to excise the whole tumor together with regional lymph nodes. The surgical specimen should contain at least 12 lymph nodes (27,28). Chang et al. (29) reported that the number of involved lymph nodes was significantly associated with survival and that lymph node involvement was an independent poor prognostic factor. Dulk et al. (19) also reported that lymph node involvement was significantly associated

with overall survival. In our study, the number of lymph nodes removed was more than 12 in all patients who did not receive neoadjuvant CRT. The mean number of lymph nodes removed in these patients was 26 ± 2 . When the patients were divided into two according to the number of removed lymph nodes as over and below 12, there was no statistically significant difference between the two groups in terms of the overall survival.

Lymph node assessment is an important prognostic factor in patients with colorectal cancer. There is an inverse relationship between the number of positive lymph nodes and prognosis (30). In our study, the mean of metastatic lymphadenopathy (LAP) / Total LAP ratio was 0.14 ± 0.03 . Univariate survival analysis revealed a statistically significant correlation between metastatic LAP / total LAP ratio and survival.

Perineural invasion is characterized by invasion of the perineural space by tumor cells. In their study with a total of 249 patients, Liebig et al. determined perineural invasion in 30% of colon cancer patients and 19% of rectal cancer patients. They found a significant statistical relationship between perineural invasion and high tumor stage and concomitant tumor metastasis. Perineural invasion has also been shown to be an independent predictor of survival (31). In our study, there was no association between perineural invasion and the overall survival.

In the literature, there was no significant difference between lymphovascular invasion-positive and -negative groups in terms of liver, lung, peritoneum and bone metastasis, while the spread to the systemic lymph node was found to be significantly higher in the lymphovascular invasion-positive group. In addition, postoperative lymph node recurrence was more frequent in this patient group (32). In our study, there was no statistically significant relationship between the presence of lymphovascular invasion and overall survival.

Maintaining bowel continuity is desirable for every patient, but the primary aim in rectum cancer is to act in accordance to oncological surgery principles. Sphincter preserving surgery may be a secondary aim. Distal and radial resection margins are critical for the surgical success. It was believed that at least a 5 cm clean distal border was needed in patients with lower rectal cancers. Thus, most of these patients had undergone APR. However, previous studies, in which the distal border was left as short as 1 cm, showed that local recurrence did not increase (33, 34). Nowadays, rectal cancer surgery is considered to be sufficient for resection with a clean distal border of 2 cm below the tumor. The distal intramural extension is limited to a 2 cm distal of the tumor unless the tumor is poorly differentiated or is diffuse metastatic (35). Wolmark et al. showed that there was no difference in survival and local recurrence between the patient groups having a distal rectal border of 2 cm or 3 cm (33). In the study by Macadam et al (36), the surgical margin was found to be negative in 81% of all resections and 86% of potentially curative resections. Among the patients included in our

study, the distal surgical margin was shorter than 2 cm in 22 (31%) patients. In our study, the distal surgical margin was positive in only one patient. Furthermore, there was no significant difference in terms of local recurrence and overall survival between the patient groups having a distance to the closest distal surgical margin of shorter and longer than 2 cm.

Cerottin et al. (37) reported that the presence of poor differentiation in the histopathological examination was a poor prognostic factor. In our study, the tumor was histopathologically poorly differentiated in 18 (26%) patients. When the patients included in the study were divided into two groups as poor and intermediate-well differentiated, there was no significant difference between the groups in terms of overall survival.

Davila et al. (38) investigated the early postoperative mortality in 32621 colorectal cancer patients and reported an early mortality rate of 4.7% between 1987 and 1988, and 3.9% between 1998 and 2000. In our study, 4 of our patients died early and the early postoperative mortality rate was 5.7%.

CONCLUSION

In conclusion, according to the results of the multivariate analyses, we found that the ASA score height, final stage of the tumor and existence of vascular (venous) invasion were significantly associated with overall survival. We concluded that the determination of these prognostic factors would be important in planning the management. Further, large-scale, randomized, controlled clinical trials are needed to clarify this issue.

Limitations of the study

There are some limitations of our study. First, it is a retrospective study. Besides, the relatively low number of cases enrolled and the short follow-up period, the unstandardized pathology results, the differences in the patients' follow-up and the patients lost during the follow-up period are the other limitations.

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